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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,378	LI ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28 and 30-74* is/are pending in the application.

4a) Of the above claim(s) *31-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on November 10, 2008 is acknowledged and has been entered. Claims 1, 3, 6, 7, 22 and 25 have been amended. Claim 29 has been canceled. Claims 1-28 and 30 are pending. Claims 31-74 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 1-28 and 30 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL.

Previous Grounds of Rejection

Claim Interpretation

The claims are drawn to a chip comprising oligonucleotide probes that comprise at least 10 nucleotides complementary to a particular nucleotide sequence. Therefore, the claims will be given a broad interpretation based specifically on the "at least 10 nucleotides" limitation. For example, Fodor will be applied broadly over the majority of the claims because the reference

teaches an array comprising all possible 10-mers, which therefore would inherently include those sequences which are specific for SARS-CoV, non-SARS-CoV, etc.

The term “SARS-like symptoms” is not explicitly defined in the specification. Instead, the term is referred in general terms, such as “The main symptoms for SARS patients include fever (greater than 38° C.), headache, body aches. After 2-7 days of illness, patients may develop a dry, nonproductive cough that may be accompanied with breathing difficulty (p. 1, lines 10-13)”. Furthermore, while certain viruses were listed as organisms capable of causing “SARS-like symptoms” (p. 42, see also Table 15), due to the breadth of the term “SARS-like” and the generality of the symptoms listed above, the term is being given the broadest reasonable interpretation as reading on any organism that causes symptoms such as fever and headaches.

The term “organism damaging the human immune system” is not explicitly defined in the specification. Instead, the term is referred to as "In some embodiments, the non-SARS-CoV infectious organism is an infectious organism damaging an infectious host's immune system. Such organism includes, but not limited to, a hepatitis virus, a transfusion transmitting virus (TTV), a human immunodeficiency virus (HIV), a parvovirus, a human cytomegalovirus (HCMV), an Epstein-Barr virus (EBV) and a tre-ponema palidum. The hepatitis virus can be hepatitis virus A (HAV), hepatitis virus B (HBV), hepatitis virus C (HCV), hepatitis virus D (HDV), hepatitis virus E (HEV), or hepatitis virus G (HGV) " (p. 38, see also Table 16, where a variety of organisms are listed). While certain viruses are listed as being capable of damaging the immune system, the specification also clearly states that the list is “not limited to” these choices. Therefore, due to the lack of explicit definition or further information regarding what contitutes "damage", the term will be interpreted as reading on any virus.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-22 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 10/556182 (the ''182 application' herein). Although the conflicting claims are not identical, they are not patentably distinct from each other because while the claims are not identical, the claims of the copending application are directed to obvious variants of the instant claims. The claims of the instant case and the copending claims are nearly identical. The difference lies in the inclusion of limitations in a different order in the two sets of claims. For example, claim 1 of the copending application is directed to a chip for assaying SARS-CoV which incorporates at least two probes which comprise at least 10 nucleotides complementary to at least two different

sequences of SARS-CoV, while the instant claim 1 is directed to a chip for assaying SARS-CoV which incorporates a probe which comprise at least 10 nucleotides complementary to SARS-CoV and one or more other probes which are complementary to a nucleotide sequence of a non-SARS-CoV infectious organism. However, it is noted that these differing limitations between the instant case and the copending '182 application, are in fact present in different claims. In the instant case, claim 2 is directed to at least two oligonucleotides complementary to two different SARS-CoV sequences, as required in claim 1 of the copending application. In the copending application, claim 19 is directed to an oligonucleotide probe complementary to a nucleotide sequence of a coronavirus not related to SARS-CoV, as required in the instant claim 1. The remaining dependent limitations to conserved and variable regions of the SARS-CoV genome are shared almost verbatim between the two copending applications and therefore the claims are obvious over the copending '182 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-8, 21 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor et al. (US Patent 6,355,432; March 2002). Fodor teaches an oligonucleotide array or chip comprising every possible 10-mer (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides).

With regard to claim 1, Fodor teaches a chip for assaying for a coronavirus causing the severe acute respiratory syndrome (SARS-CoV) and a non-SARS-CoV infectious organism, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon an oligonucleotide probe complementary to a nucleotide sequence of SARS-CoV genome, said nucleotide sequence comprising at least 10 nucleotides, and one or more of the following oligonucleotide probe(s) (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences):

a) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism causing SARS-like symptoms, said nucleotide sequence comprising at least 10 nucleotides (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences);

b) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism damaging an infectious host's immune system, said nucleotide sequence comprising at least 10 nucleotides (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 2, Fodor teaches an embodiment of claim 1, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon at least two oligonucleotide probes complementary to at least two different nucleotide sequences of SARS-CoV genome, each of said two different nucleotide sequences comprising at least 10 nucleotides (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 3, Fodor teaches an embodiment of claim 2, wherein the at least two different nucleotide sequences of SARS-CoV genome comprises:

a) a nucleotide sequence of at least 10 nucleotides located within a conserved region of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a variable region of SARS-CoV genome (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences); or

b) a nucleotide sequence of at least 10 nucleotides located within a structural protein coding gene of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a non-structural protein coding gene of SARS-CoV genome (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 4, Fodor teaches an embodiment of claim 2, which further comprises:

a) at least one of the following three oligonucleotide probes: an immobilization control probe

that is labeled and does not participate in any hybridization reaction when a sample containing or suspected of containing of a SARS-CoV or a non-SARS-CoV infectious organism is contacted with the chip, a positive control probe that is not complementary to any sequence of a SAKS-CoV or non-SARS-CoV infectious organism but is complementary to a sequence contained in the sample not found in the SARS-CoV or the non-SARS-CoV infectious organism and a negative control probe that is not complementary to any nucleotide sequence contained in the sample (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences; and also col. 24, lines 15-19, where hybridization controls are included); and
b) a blank spot (col. 24, lines 15-19, where hybridization controls are included).

With regard to claim 5, Fodor teaches an embodiment of claim 2, which comprises at least two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides, respectively, located within a conserved region of SARS-CoV genome, located within a structural protein coding gene of SARS-CoV genome or located within a non-structural protein coding gene of SARS-CoV genome (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 6, Fodor teaches an embodiment of claim 2, wherein:
a) the conserved region of S ARS-CoV genome is a region located within the Replicase 1A or 1B gene or the Nucleocapsid (N-) gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences);

b) the structural protein coding gene of SARS-CoV genome is a gene encoding the Spike glycoprotein (S), the small envelope protein (E) or the Nucleocapsid protein (N); or c) the non-structural protein coding gene of SARS-CoV genome is a gene encoding the Replicase 1A or 1B (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 7, Fodor teaches an embodiment of claim 3, wherein the variable region of SARS-CoV genome is a region located within the Spike glycoprotein (S) gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 8, Fodor teaches an embodiment of claim 2, which comprises at least two of the following four oligonucleotide probes: two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides located within the Replicase 1A or 1B gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence of at least 10 nucleotides located within the N gene of SAKS-CoV and an oligonucleotide probe complementary to a nucleotide sequence of at least 10 nucleotides located within the S gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 21, Fodor teaches an embodiment of claim 2, wherein at least one of the oligonucleotide probes is complementary to a highly expressed nucleotide sequence of

SARS-CoV genome (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 30, Fodor teaches an embodiment of claim 1, wherein the support comprises a surface that is selected from the group consisting of a silicon, a plastic, a glass, a ceramic, a rubber, and a polymer surface (col. 36, lines 23-27, where the substrate comprises silicon).

The rejection below has been adjusted to properly refer to the author's last name, Shi, as noted by Applicant.

Claims 1-8, 15, 21 and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Si et al. (Chinese Science Bulletin, June 2003, vol. 48, no. 12, p. 1165-1169) as evidenced by Marra et al. (Science, 2003, vol. 300, p. 1399-1404; epub May 2003). Shi teaches an oligonucleotide microarray in SARS coronavirus detection (Abstract).

With regard to claim 1, Shi teaches a chip for assaying for a coronavirus causing the severe acute respiratory syndrome (SARS-CoV) and a non-SARS-CoV infectious organism, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon an oligonucleotide probe complementary to a nucleotide sequence of SARS-CoV genome, said nucleotide sequence comprising at least 10 nucleotides, and one or more of the following oligonucleotide probe(s) (p. 1168, col. 2, ‘design of the oligos and microarray’ heading, Figure 1 and Table 1, where the specific oligonucleotide sequences complementary to SARS-CoV are included):

a) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism causing SARS-like symptoms, said nucleotide sequence comprising at least 10 nucleotides (Table 1, where oligo10 is a sequence that is complementary to multiple non-SARS-CoV organisms, including bovine coronavirus, rat coronavirus and avian infectious bronchitis virus);

b) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism damaging the human's immune system, said nucleotide sequence comprising at least 10 nucleotides (Table 1, where oligo 10 is a sequence that is complementary to multiple non-SARS-CoV organisms, including bovine coronavirus, rat coronavirus and avian infectious bronchitis virus).

With regard to claim 2, Shi teaches an embodiment of claim 1, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon at least two o!igonucleotide probes complementary to at least two different nucleotide sequences of SARS-CoV genome, each of said two different nucleotide sequences comprising at least 10 nucleotides (p. 1168, col. 2, ‘design of the oligos and microarray’ heading, Figure 1 and Table 1, where the specific oligonucleotide sequences complementary to SARS-CoV are included).

With regard to claim 3, Shi teaches an embodiment of claim 2, wherein the at least two different nucleotide sequences of SARS-CoV genome comprises:

a) a nucleotide sequence of at least 10 nucleotides located within a conserved region of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a variable region of SARS-CoV genome (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls

between 265-13,398, which is a conserved region, p. 1401, col. 2); or

b) a nucleotide sequence of at least 10 nucleotides located within a structural protein coding gene of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a non-structural protein coding gene of SARS-CoV genome (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398, which is a conserved region, p. 1401, col. 2).

With regard to claim 4, Shi teaches an embodiment of claim 2, which further comprises:

a) at least one of the following three oligonucleotide probes: an immobilization control probe that is labeled and does not participate in any hybridization reaction when a sample containing or suspected of containing of a SARS-CoV or a non-SARS-CoV infectious organism is contacted with the chip, a positive control probe that is not complementary to any sequence of a SAKS-CoV or non-SARS-CoV infectious organism but is complementary to a sequence contained <u>in</u> the sample not found in the SARS-CoV or the non-SARS-CoV infectious organism and a negative control probe that is not complementary to any nucleotide sequence contained in the sample (Figure 1, where there were negative control spots included); and

b) a blank spot (Figure 1, where there were empty control spots or blank spots).

With regard to claim 5, Shi teaches an embodiment of claim 2, which comprises at least two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides, respectively, located within a conserved region of SARS-CoV genome, located within a structural protein coding gene of SARS-CoV genome or located within a non-structural protein coding gene of SARS-CoV genome (p. 1168, col. 2, ‘design of the oligos and microarray’ heading, Figure 1 and Table 1, where the specific oligonucleotide sequences

complementary to SARS-CoV are included; Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398, which is a conserved region, p. 1401, col. 2).

With regard to claim 6, Shi teaches an embodiment of claim 5, wherein:
a) the conserved region of S ARS-CoV genome is a region located within the Replicase 1A or 1B gene or the Nucleocapsid (N-) gene of SARS-CoV;
b) the structural protein coding gene of SARS-CoV genome is a gene encoding the Spike glycoprotein (S), the small envelope protein (E) or the Nucleocapsid protein (N); or c) the non-structural protein coding gene of SARS-CoV genome is a gene encoding the Replicase 1A or 1B (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398, which is a conserved region, p. 1401, col. 2).

With regard to claim 7, Shi teaches an embodiment of claim 3, wherein the variable region of SARS-CoV genome is a region located within the Spike glycoprotein (S) gene of SARS-CoV (Table 1, oligo 28 and oligo 05, which are directed to spike glycoprotein, as evidenced by Marra et al., Figure 1, where the Spike glycoprotein falls between 21,492-25,259).

With regard to claim 8, Shi teaches an embodiment of claim 2, which comprises at least two of the following four oligonucleotide probes: two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides located within the Replicase 1A or 1B gene of SARS-CoV (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398), an oligonucleotide probe complementary to a nucleotide sequence of at least 10

nucleotides located within the N gene of SAKS-CoV and an oligonucleotide probe complementary to a nucleotide sequence of at least 10 nucleotides located within the S gene of SARS-CoV (Table 1, oligo 28 and oligo 05, which are directed to spike glycoprotein, as evidenced by Marra et al., Figure 1, where the Spike glycoprotein falls between 21,492-25,259).

With regard to claim 15, Shi teaches an embodiment of claim 4, wherein the label of the immobilization control probe is selected from the group consisting of a chemical, an enzymatic, an immunogenic, a radioactive, a fluorescent, a luminescent and a FRET label (p. 1166, col. 2, where the cDNAs were fluorescently labeled).

With regard to claim 21, Shi teaches an embodiment of claim 2, wherein at least one of the oligonucleotide probes is complementary to a highly expressed nucleotide sequence of SARS-CoV genome (p. 1168, col. 2, ‘design of the oligos and microarray’ heading, Figure 1 and Table 1, where the specific oligonucleotide sequences complementary to SARS-CoV are included).

With regard to claim 30, Shi teaches an embodiment of claim 1, wherein the support comprises a surface that is selected from the group consisting of a silicon, a plastic, a glass, a ceramic, a rubber, and a polymer surface (p. 1168, col. 1, ‘preparation of the 60-mer oligonucleotide microarray heading’ where silanized slides were coated with poly lysine prior to the addition of oligonucleotide probes).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Ruan et al. (2003, The Lancet, 361(9371): 1779-85).

While Fodor teaches an oligonucleotide array or chip comprising every possible 10-mer (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides), Fodor does not explicitly teach the sequence of SEQ ID NO:229 below.

With regard to claim 9, Ruan teaches an embodiment of claim 8, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a Replicase 1A or 1B nucleotide sequence, or a

complementary strand thereof, that is SEQ ID NO:210 (see alignment below, between SEQ ID NO:210 and AY283798); or

```
Query  1     TCATAGCTAACATCTTTACTCCTCTTGTGCAACCTGTGGGTGCTTTAGATGTGTCTGCTT  60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  9256  TCATAGCTAACATCTTTACTCCTCTTGTGCAACCTGTGGGTGCTTTAGATGTGTCTGCTT
9315

Query  61    CAGTAGTGGC  70
             ||||||||||
Sbjct  9316  CAGTAGTGGC  9325
```

b) has at least 90% identity to a Replicase 1A or 1B nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:210 (see alignment above, between SEQ ID NO:210 and AY283798).

With regard to claim 10, Ruan teaches an embodiment of claim 9, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:210 (see alignment above, between SEQ ID NO:210 and AY283798).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Briese et al. (US PgPub 20040265796; December 2004, 102(e) date April 17, 2003).

While Fodor teaches an oligonucleotide array or chip comprising every possible 10-mer (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides), Fodor does not explicitly teach the sequence of SEQ ID NO:229 below.

With regard to claim 11, Briese teaches an embodiment of claim 8, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a N nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:225 (see alignment below between SEQ ID NO:1 of Briese and with SEQ ID NO:225); or

```
Qy          1 GAGGTGGTGAAACTGCCCTCGCGCTATTGCTGCTAGACAGATTGAACCAGCTTGAGAGCA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        255 GAGGTGGTGAAACTGCCCTCGCGCTATTGCTGCTAGACAGATTGAACCAGCTTGAGAGCA
314

Qy         61 AAGTTTCTGG 70
              ||||||||||
Db        315 AAGTTTCTGG 324
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b) has at least 90% identity to a N nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:225 (see alignment above between SEQ ID NO:1 of Briese and with SEQ ID NO:225).

With regard to claim 12, Briese teaches an embodiment of claim 11, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:225 (see alignment above between SEQ ID NO:1 of Briese and with SEQ ID NO:225).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Vilalta et al. (WO2005021707; March 2005; with priority to 60/470820, effective date May 16, 2003).

While Fodor teaches an oligonucleotide array or chip comprising every possible 10-mer (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides), Fodor does not explicitly teach the sequence of SEQ ID NO:229 below.

With regard to claim 13, Vilalta teaches an embodiment of claim 8, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a S nucleotide sequence, or a complementary strand thereof, that is set forth in SEQ ID NO:229 (see alignment below between SEQ ID NO:3 of Vilalta); or

```
Qy          1 CACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATATCAAGATGTTAACTGCACTG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1754 CACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATATCAAGATGTTAACTGCACTG
1813

Qy         61 ATGTTTCTAC 70
              ||||||||||
Db       1814 ATGTTTCTAC 1823
```

b) has at least 90% identity to a S nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:229 (see alignment above between SEQ ID NO:3 of Vilalta).

With regard to claim 14, Vilalta teaches an embodiment of claim 13, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:229 (see alignment above between SEQ ID NO:3 of Vilalta).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Martoglio et al. (Molecular Medicine, 2000, 6(9):750-765).

With regard to claim 18, Fodor teaches an embodiment of claim 8, which comprises two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV, an oligonucleotide probe complementary to a

nucleotide sequence located within the N gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences), an immobilization control probe that is labeled and does not participate in any hybridization reaction when a sample containing or suspected of containing of a SARS-CoV or a non-SARS-CoV infectious organism is contacted with the chip, a positive control probe that is not complementary to any sequence of a SARS-CoV or non-SARS-CoV infectious organism but is complementary to a sequence contained in the sample not found in the SARS-CoV or the non-SARS-CoV infectious organism and a negative control probe that is not complementary to any nucleotide sequence contained in the sample (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences; also col. 24, lines 15-19, where hybridization controls are included).

With regard to claim 19, Fodor teaches an embodiment of claim 18, which comprises multiple spots of the two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1B gene of SAKS-CoV, the oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV, the oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these

sequences), the immobilization control probe, the positive control probe and the negative control probe (col. 24, lines 15-19, where hybridization controls are included).

Regarding claims 16-17, Fodor does not teach the spiking of a non-SARS-CoV sequence in the sample and also does not teach that the sequence is of Arabidopsis origin. Regarding claims 18 and 19, Fodor does not teach the inclusion of an immobilization control probe or a positive control probe. Martoglio teaches the inclusion of these probes in a microarray format.

With regard to claim 16-17, Martoglio teaches spiking a non-SARS-CoV sequence in the sample to be assayed and that the sequence is of Arabidopsis origin (p. 752, col. 1-2, where the samples were spiked with an Arabidopsis cytochrome cDNA as a control for labeling and hybridization; see also p. 753, 'processing hybridization signals' heading).

With regard to claim 18-19, Martoglio teaches an immobilization control probe and a positive control probe (p. 752, col. 1-2, where the samples were spiked with an Arabidopsis cytochrome cDNA as a control for labeling and hybridization; see also p. 753, 'processing hybridization signals' heading).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included the additional controls for microarray normalization taught by Martoglio to the array for SARS-CoV sequences taught by Fodor to arrive at the claimed invention with a reasonable expectation for success. As taught by Martoglio, "To account for potential differences in probe labeling, each data set was normalized with respect to the corresponding mean signal intensity of *Arabidopsis thaliana* cytochrome c554 cDNA added to each probe as direct internal controls, as described above" (p. 753, 'processing hybridization signals' heading). Therefore, one of ordinary skill in the art at the time the invention was made

would have been motivated to have included the additional controls for microarray normalization taught by Martoglio to the array for SARS-CoV sequences taught by Fodor to arrive at the claimed invention with a reasonable expectation for success.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Saiki et al. (PNAS, 1989, vol. 86, p. 6230-6234).

With regard to claim 20, Saiki teaches an embodiment of claim 4, wherein at least one of the oligonucleotide probe comprises, at its 5' end, a poly dT region to enhance its immobilization on the support (p. 6230, ‘tailing of oligonucleotides’ heading, where the oligos were tailed with poly dT prior to immobilization).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the teachings of tailed oligonucleotides to the 10-mer array or chip of Fodor to arrive at the claimed invention with a reasonable expectation for success. As taught by Saiki, “in a single hybridization reaction, an entire series of sequences could be examined simultaneously”. Saiki also teaches “the poly(dT) tail would be a larger target for UV crosslinking and should preferentially react with the nylon" (p. 6230, col. 1). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have incorporated the teachings of tailed oligonucleotides to the 10-mer array or chip of Fodor to arrive at the claimed invention with a reasonable expectation for success.

The typographical error in the motivation statement has been corrected to refer to Fodor. This typographical error did not appear to cause confusion.

Claims 22-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Marra et al. (Science, 2003, vol. 300, p. 1399-1404; epub May 2003).

With regard to claim 22-23, Marra teaches an embodiment of claim 1, wherein the non-SARS-CoV infectious organism causing SARS-Iike symptoms is selected from the group consisting of a human coronavirus 229E, a human coronavirus 0C43, a human enteric coronavirus, an influenza virus, a parainfluenza virus, a respiratory sncytical virus, a human metapneumovirus, a rhinovirus, an adenovirus, a mycoplasma pneumoniae, a chlamydia pneumoniae, a measles virus and a rubella virus (Figure 1, legend, where human coronavirus was included in the listing).

With regard to claim 24, Marra teaches an embodiment of claim 22, wherein the parainfluenza virus is selected from the group consisting of parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3 and parainfluenza virus 4 (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

With regard to claim 25, 27, 28, Marra teaches an embodiment of claim 1, wherein the non-SARS-CoV infectious organism damaging an infectious host's immune system is selected from the group consisting of a hepatitis virus, a transfusion transmitting virus (TTV), a human immunodeficieney virus (HIV), a parvovirus, a human cytomegalovirus (HCMV), an Epstein-Barr virus (EBV) and a Treponema palidum (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

With regard to claim 26, Marra teaches an embodiment of claim 25, wherein the hepatitis virus is selected from the group consisting of hepatitis virus A (HAV), hepatitis virus B (HBV), hepatitis virus C (HCV), hepatitis virus D (HDV), hepatitis virus E (HEV) and hepatitis virus G (HGV) (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Fodor to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success. While Marra does not teach the inclusion of these various non-SARS-CoV organisms in a microarray format, Marra does establish the phylogenetic relationship between the SARS-CoV genome, and particular coding features within the genome as compared to these non-SARS-CoV sequences. As Fodor already includes a probe complementary to a non-SARS-CoV sequence, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Fodor to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success.

Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi as applied to claims 1-8, 15, 21 and 30 above and further in view of Ruan et al. (2003, The Lancet, 361(9371): 1779-85).

While Rong teaches probes that hybridize with the SARS-CoV genome, Shi does not teach the specific sequence as claimed below.

With regard to claim 9, Ruan teaches an embodiment of claim 8, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a Replicase 1A or 1B nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:210 (see alignment below, between SEQ ID NO:210 and AY283798); or

```
Query  1     TCATAGCTAACATCTTTACTCCTCTTGTGCAACCTGTGGGTGCTTTAGATGTGTCTGCTT  60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  9256  TCATAGCTAACATCTTTACTCCTCTTGTGCAACCTGTGGGTGCTTTAGATGTGTCTGCTT
9315

Query  61    CAGTAGTGGC  70
             ||||||||||
Sbjct  9316  CAGTAGTGGC  9325
```

b) has at least 90% identity to a Replicase 1A or 1B nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:210 (see alignment above, between SEQ ID NO:210 and AY283798).

With regard to claim 10, Ruan teaches an embodiment of claim 9, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:210 (see alignment above, between SEQ ID NO:210 and AY283798).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound.

Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi as applied to claims 1-8, 15, 21 and 30 above and further in view of Briese et al. (US PgPub 20040265796; December 2004, 102(e) date April 17, 2003).

While Shi teaches probes that hybridize with the SARS-CoV genome, Shi does not teach the specific sequence as claimed below.

With regard to claim 11, Briese teaches an embodiment of claim 8, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a N nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:225 (see alignment below between SEQ ID NO:1 of Briese and with SEQ ID NO:225); or

```
Qy          1 GAGGTGGTGAAACTGCCCTCGCGCTATTGCTGCTAGACAGATTGAACCAGCTTGAGAGCA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        255 GAGGTGGTGAAACTGCCCTCGCGCTATTGCTGCTAGACAGATTGAACCAGCTTGAGAGCA 314

Qy         61 AAGTTTCTGG 70
              ||||||||||
Db        315 AAGTTTCTGG 324
```

b) has at least 90% identity to a N nucleotide sequence comprising a nucleotide sequence, or a

complementary strand thereof, that is SEQ ID NO:225 (see alignment above between SEQ ID NO:1 of Briese and with SEQ ID NO:225).

With regard to claim 12, Briese teaches an embodiment of claim 11, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:225 (see alignment above between SEQ ID NO:1 of Briese and with SEQ ID NO:225).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi as applied to claims 1-8, 15, 21 and 30 above and further in view of Vilalta et al. (WO2005021707; March 2005; with priority to 60/470820, effective date May 16, 2003).

While Rong teaches probes that hybridize with the SARS-CoV genome, Rong does not teach the specific sequence as claimed below.

With regard to claim 13, Vilalta teaches an embodiment of claim 8, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a S nucleotide sequence, or a complementary strand thereof, that is set forth in SEQ ID NO:229 (see alignment below between SEQ ID NO:3 of Vilalta); or

```
Qy          1 CACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATATCAAGATGTTAACTGCACTG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1754 CACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATATCAAGATGTTAACTGCACTG 1813

Qy         61 ATGTTTCTAC 70
              ||||||||||
Db       1814 ATGTTTCTAC 1823
```

b) has at least 90% identity to a S nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:229 (see alignment above between SEQ ID NO:3 of Vilalta).

With regard to claim 14, Vilalta teaches an embodiment of claim 13, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:229 (see alignment above between SEQ ID NO:3 of Vilalta).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound.

Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi as applied to claims 1-8, 15, 21 and 30 above and further in view of Martoglio et al. (Molecular Medicine, 2000, 6(9):750-765).

With regard to claim 18, Shi teaches an embodiment of claim 8, which comprises two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398), an oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV (Table 1, oligo 27 and oligo 18, which are directed to the nucleocapsid or N gene, as evidenced by Marra, et al., Figure 1, where the N gene falls between 28,120-29,388), an oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV, a negative control probe that is not complementary to any nucleotide sequence contained in the sample (Figure 1, where there were negative control spots included and where there were empty control spots or blank spots).

With regard to claim 19, Shi teaches an embodiment of claim 18, which comprises multiple spots of the two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398), the oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV (Table 1, oligo 27 and oligo 18, which are directed to the nucleocapsid or N gene, as evidenced by Marra, et al., Figure 1, where the N gene falls between 28,120-29,388), the oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV (Table 1, oligo 28 and oligo 05, which are directed to spike glycoprotein, as evidenced by Marra et al., Figure 1, where the Spike glycoprotein falls between 21,492-25,259), and the negative control probe (Figure 1, where there were negative control spots included and where there were empty control spots or blank spots).

Regarding claims 16-17, Shi does not teach the spiking of a non-SARS-CoV sequence in the sample and also does not teach that the sequence is of Arabidopsis origin. Regarding claims 18 and 19, Shi does not teach the inclusion of an immobilization control probe or a positive control probe. Martoglio teaches the inclusion of these probes in a microarray format.

With regard to claim 16-17, Martloglio teaches spiking a non-SARS-CoV sequence in the sample to be assayed and that the sequence is of Arabidopsis origin (p. 752, col. 1-2, where the samples were spiked with an Arabidopsis cytochrome cDNA as a control for labeling and hybridization; see also p. 753, ‘processing hybridization signals’ heading).

With regard to claim 18-19, Martoglio teaches an immobilization control probe and a positive control probe (p. 752, col. 1-2, where the samples were spiked with an Arabidopsis cytochrome cDNA as a control for labeling and hybridization; see also p. 753, ‘processing hybridization signals’ heading).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included the additional controls for microarray normalization taught by Martoglio to the array for SARS-CoV sequences taught by Shi to arrive at the claimed invention with a reasonable expectation for success. As taught by Martoglio, “To account for potential differences in probe labeling, each data set was normalized with respect to the corresponding mean signal intensity of *Arabidopsis thaliana* cytochrome c554 cDNA added to each probe as direct internal controls, as described above” (p. 753, ‘processing hybridization signals' heading). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have included the additional controls for microarray normalization taught by Martoglio to the array for SARS-CoV sequences taught by Shi to arrive at the claimed invention with a reasonable expectation for success.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shi as applied to claims 1-8, 21 and 30 above and further in view of Saiki et al. (PNAS, 1989, vol. 86, p. 6230-6234).

With regard to claim 20, Saiki teaches an embodiment of claim 4, wherein at least one of the oligonucleotide probe comprises, at its 5' end, a poly dT region to enhance its immobilization

on the support (p. 6230, ‘tailing of oligonucleotides’ heading, where the oligos were tailed with poly dT prior to immobilization).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the teachings of tailed oligonucleotides to the array or chip of Shi to arrive at the claimed invention with a reasonable expectation for success. As taught by Saiki, “in a single hybridization reaction, an entire series of sequences could be examined simultaneously”. Saiki also teaches “the poly(dT) tail would be a larger target for UV crosslinking and should preferentially react with the nylon" (p. 6230, col. 1). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have incorporated the teachings of tailed oligonucleotides to the array or chip of Shi to arrive at the claimed invention with a reasonable expectation for success.

Claims 22-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi as applied to claims 1-8, 15, 21 and 30 above and further in view of Marra et al. (Science, 2003, vol. 300, p. 1399-1404; epub May 2003).

With regard to claim 22-23, Marra teaches an embodiment of claim 1, wherein the non-SARS-CoV infectious organism causing SARS-like symptoms is selected from the group consisting of a human coronavirus 229E, a human coronavirus 0C43, a human enteric coronavirus, an influenza virus, a parainfluenza virus, a respiratory sncytical virus, a human metapneumovirus, a rhinovirus, an adenoviruse, a mycoplasma pneumoniae, a chlamydia pneumoniae, a measles virus and a rubella virus (Figure 1, legend, where human coronavirus was included in the listing).

With regard to claim 24, Marra teaches an embodiment of claim 22, wherein the parainfluenza virus is selected from the group consisting of parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3 and parainfluenza virus 4 (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

With regard to claim 25, 27, 28, Marra teaches an embodiment of claim 1, wherein the non-SARS-CoV infectious organism damaging an infectious host's immune system is selected from the group consisting of a hepatitis virus, a transfusion transmitting virus (TTV), a human immunodeficieney virus (HIV), a parvovirus, a human cytomegalovirus (HCMV), an Epstein-Barr virus (EBV) and and Treponema palidum (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

With regard to claim 26, Marra teaches an embodiment of claim 25, wherein the hepatitis virus is selected from the group consisting of hepatitis virus A (HAV), hepatitis virus B (HBV), hepatitis virus C (HCV), hepatitis virus D (HDV), hepatitis virus E (HEV) and hepatitis virus G (HGV) (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Shi to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success. While Marra does not teach the inclusion of these various non-SARS-CoV organisms in a microarray format, Marra does establish the phylogenetic relationship between the SARS-CoV genome, and particular coding features within the genome as compared to these non-SARS-CoV sequences. As Shi already includes a probe

complementary to a non-SARS-CoV sequence, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Shi to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success.

Response to arguments

Applicant's arguments filed November 10, 2008 have been fully considered but they are not persuasive.

Applicant requests that the rejection of claims 1-22 and 30 as being unpatentable over claims 1-23 of copending application 10/556182 be held in abeyance. Applicant's arguments are fully considered and found unpersuasive because these are not the only remaining rejections in this application. As discussed above, the rejections under 35 U.S.C. 103(a) are still pending. Therefore, the rejections under provisional double patenting are maintained until the issues are resolved.

Applicant traverses the rejection of claims 1-8, 21 and 30 as being anticipated by Fodor. Applicant argues that Fodor "does not teach any SARS or non-SARS specific oligonucleotide; nor does it teach any specific oligonucleotide sequences at all". Applicant also states "Fodor briefly discloses a genus of 10-mer oligonucleotides that encompass over a million distinct species" and points to MPEP 2131.02 as teaching that "a genus does not always anticipate a claim to a species". Applicant argues "when a compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g. select

various substituents from a list of alternatives" (p. 19 of remarks). Regarding the instant teaching of Fodor, Applicant concludes "much like In re Petering, Fodor merely discloses a genus encompassing a vast number (>10^6) of oligonucleotides having a general formula of $(A/T/C/G)_{10}$.

Regarding the issue of anticipation, Applicant argues "the law of inherent anticipation does not extend so far as to vitiate the common principles of genus-species anticipation". Applicant again quotes the MPEP 2112 stating "an invitation to investigate is not an inherent disclosure" where a prior art reference "discloses no more than a broad genus of potentiatl applications of its own discoveries" (p. 20 of remarks).

While Applicant's arguments regarding the size of the genus of probes taught by Fodor are noted, these arguments are not persuasive. Fodor teaches an array comprising every 10-mer placed on an array and therefore would inherently include the sequences encompassed by the instant claims. The comparison to *In re Petering* is not apt or particularly relevant because, unlike a compound with multiple different R-groups selected from a list, placed around a central structure, there is no picking and choosing of sequence elements necessary for the array produced by Fodor to anticipate the instant claims. The only step necessary for one of ordinary skill to "at once envisage" the sequences on the array which are complementary to SARS or non-SARS sequences would be to select the probes through hybridization to a SARS specific sequence. The probes on the microarray of Fodor which anticipate the instantly claimed array are present without extra investigation or experimentation. In the absence of additional limitations which would exclude Fodor, Fodor anticipates the instantly claimed array for the reasons stated above. The rejection is maintained.

Applicant traverses the rejection of claims 1-8, 15, 21 and 30 are rejected as being anticipated by Shi as evidenced by Marra. Applicant argues “Claim 1 as amended no longer recites an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV coronaviridae virus" and note that all of the rejected claims incorporate the limitations of claim 1. Applicant asserts simply “each of the non-SARS-CoV organisms taught in Shi belongs to the category non-SARS-CoV coronaviridae viruses, which is no longer recited in claim 1 as amended" and concludes "Shi does not teach a SARS diagnostic chip comprising one or more oligonucleotide probe(s) complementary to a nucleotide sequence of any of the non-SARS-CoV infectious organisms recited in claim 1 as amended" (p. 21 of remarks).

These arguments are not persuasive. As noted in the art rejection stated above, claim 1 is rejected over Shi as evidenced by Marra as comprising probes complementary not just to the non-SARS-CoV coronaviridae virus, but also to the broadly stated “non-SARS-CoV infectious organism causing SARS-like symptoms” (a) and "non-SARS-CoV infectious organism damaging the human's immune system" (b) (p. 21 of remarks) . Applicant did not argue these two features of the claim and simply states that the non-SARS CoV organisms taught by Shi belong to non-SARS-CoV organisms, but does not distinguish Shi's teaching over the organisms of a) or b). Therefore, because of the breadth of "SARS-like symptoms" and "damaging the human immune system", combined with the lack of definition of either term (as stated in the claim interpretation above), the claims remain rejected over the teachings of Shi. The rejection is maintained.

Applicant traverses the rejection of claims 9 and 10 as being unpatentable over Fodor and Ruan. Applicant asserts "the main problem with Fodor is that it discloses a very large (>10^6) genus of oligonucleotides of a general formula (A/T/C/G)10, but does not teach any specific nucleotide sequence, SARS-CoV or non-SARS-CoV" and notes "the existence of SARS-CoV was not even known at the time of Fodor's issuance" (p. 23 of remarks). Applicant also argues "the fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a prima facie case of obviousness" And "to establish a prima facie case of obviousness in a genus-species situation such as this, the Office needs to consider a number of factors including, inter alia, the size of the genus, the structural similarity, the teachings of similar properties or uses, and so forth". Applicant concludes by noting that "obviousness cannot be predicated on what is not known at the time an invention is made" (p. 23).

These arguments have been carefully considered but are not persuasive. First, as noted in the response above, while the genus of probes taught by Fodor is large, Fodor teaches an array comprising ***every*** 10-mer placed on an array and therefore would inherently include the sequences encompassed by the instant claims (emphasis added). The size of the genus of probes attached to Fodor's array does not change the fact that the array of Fodor comprises the sequences claimed and the instantly claimed substrate is therefore anticipated. Furthermore, in response to Applicant's arguments regarding the portion of the MPEP that notes that obviousness cannot be based on what is not known, these arguments are also not persuasive. The array of Fodor comprises all 10-mer sequences and therefore inherently anticipates any 10-mer sequence, including sequences that were not yet discovered or characterized at the time Fodor was issued.

Regarding the rejection of claims 9 and 10 as being obvious over a combination of Fodor and Ruan, it is noted that Applicant has not argued the features of Ruan. However, it is reiterated that Ruan renders obvious the specific probe sequence claimed because the sequence of Fodor necessarily and includes all 10-mer sequences, including those 10-mers sequence(s) within SEQ ID NO:210 as taught by Ruan. Therefore, the combination renders the claims obvious. The rejection is maintained.

Applicant traverses the rejection of claims 11 and 12 as being obvious over Fodor in view of Briese, claims 13 and 14 as being obvious over Fodor in view of Vilalta, claims 16-19 as being obvious over Fodor in view of Martoglio, and claim 20 as being obvious over Fodor in view of Saiki. Applicant summarizes the teachings of these references. Applicant argues that the combination of references does not render claims 11 and 12, claims 13 and 14, claims 16-19 and claim 19 obvious over the combination of claims, “for substantially the same reasons as set for with respect to Fodor and Ruan” and “namely, the combination… does not teach or even suggest a diagnostic chip featuring all of the limitations” of the claims. (p. 24-26 of remarks).

These arguments are not persuasive for the same reasons asserted above regarding Fodor in view of Ruan. Fodor renders obvious the diagnostic chip of the independent claims, as established in the art rejection recited above and as argued in the response above. The rejections are maintained.

Applicant traverses the rejection of claims 22-29 as being obvious over Fodor in view of Marra. Applicant argues "Marra allegedly teaches that a variety of additional viruses and

organisms are listed as related to SARS-CoV phylogenetically" and argues that the combination does not render the claimed invention obvious "for substantially the same reasons as those set forth with respect to Fodor and Ruan". Applicant also argues "the combination of Fodor and Marra does not teach or even suggest a diagnostic chip featuring all of the limitations recited in claims 22-28" (p. 28 of remarks). Applicant also states "Applicants fail to see how different infectious organisms' being grouped together in a phylogenetic tree can provide motivation to combine oligonucleotides complementary to nucleotide sequences to any of these organisms on the same diagnostic chip with a reasonable expectation for success."

These arguments are not persuasive for the same reasons asserted above regarding Fodor in view of Ruan. Fodor renders obvious the diagnostic chip of the independent claims, as established in the art rejection recited above and as argued in the response above. As noted in the art rejection, the chip comprises both SARS-specific and non-SARS specific viruses. While the terms "SARS-like symptoms" and "damaging human immune system" are broad, it is also noted that the specific viruses claimed in claims 22 and 25 are related to SARS, non-SARS coronaviruses and other viruses. Therefore it would have been obvious to extend the chip to include a variety of additional "non-SARS" viruses, including those as taught by Marra, as claimed in the broad independent claim. The rejections are maintained.

Applicant traverses the rejection of claims 9-10 as being obvious over Shi in view of Ruan. Applicant argues "claim 1 as amended no longer recites an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS CoV coronaviridae virus" and "accordingly, Shi does not teach a SARS diagnostic chip comprising one or more

oligonucleotide probe(s) complementary to a nucleotide sequence of any one of the non-SARS-CoV infectious organisms recited in claim 1 as amended". Applicant also argues, "since Ruan does not contain any teachings that would remedy this deficiency of Shi, it is apparent that the combination of Shi and Ruan does not teach or even suggest a diagnostic chip featuring all the limitations recited in claim 9 and 10" (p. 29 of remarks).

These arguments are not persuasive. As noted in the response to the arguments over Shi, above, claim 1 is rejected over Shi as evidenced by Marra as comprising probes complementary not just to the non-SARS-CoV coronaviridae virus, but also to the broadly stated "non-SARS-CoV infectious organism causing SARS-like symptoms" (a) and "non-SARS-CoV infectious organism damaging the human's immune system" (b) (p. 21 of remarks) . Applicant did not argue these two features of the claim and simply states that the non-SARS CoV organisms taught by Shi belong to non-SARS-CoV organisms, but does not distinguish Shi's teaching over the organisms of a) or b). Therefore, because of the breadth of "SARS-like symptoms" and "damaging the human immune system", combined with the lack of definition of either term (as stated in the claim interpretation above), the claims remain rejected over the teachings of Shi. The rejection is maintained.

Applicant traverses the rejection of claims 11 and 12 as being obvious over Shi and Briese, claims 13 and 14 as being obvious over Shi in view of Vilalta, claims 16-19 as being obvious over Fodor in view of Martoglio, and claim 20 as being obvious over Fodor in view of Saiki. Applicant summarizes the teachings of these references. Applicant argues that the combination of references does not render claims 11 and 12, claims 13 and 14, claims 16-19 and

claim 19 obvious over the combination of claims and references noted above, “for substantially the same reasons as set for with respect to Shi and Ruan” and “namely, the combination… does not teach or even suggest a diagnostic chip featuring all of the limitations” of the claims. (p. 29-32 of remarks).

These arguments are not persuasive for the same reasons asserted above regarding Shi and Shi in view of Ruan. Shi renders obvious the diagnostic chip of the independent claims, as established in the art rejection recited above and as argued in the response above. The rejections are maintained.

Applicant traverses the rejection of claims 22-28 as being obvious over Shi in view of Marra. Applicant argues “the combination of Shi and Marra does not render claims 22-28 obvious for substantially the same reasons as those set forth above with respect to Shi and Ruan". Applicant also argues "Shi does not teach the idea of combining SARS-CoV and non-SARS-CoV diagnostics on one chip. Shi merely teaches that oligo 10 in Table 1 is a common sequence of SARS-CoV, bovine coronavirus, murine hepatitis virus, rat coronavirus and avian infectious bronchitis virus" and "thus, it would be impossible to distinguish a SARS-CoV infection from a non-SARS coV infection using the diagnostic array of Shi" and concludes that it would not be obvious to extend this chip of Shi to include additional organisms, as taught by Marra (p. 33 of remarks).

These arguments are not persuasive. Applicant is arguing features of the invention which are not claimed. Applicant’s arguments regarding distinguishing SARS-CoV infection from non-SARS-CoV infection amounts to an intended use of the instantly claimed chip. As noted in

the art rejection over Shi, the additional probes of a)-c) are complementary to oligo10 of Shi. While the sequence of oligo10 is complementary to SARS-CoV, it is also complementary to non-SARS-CoV organisms, including those noted by Applicant, which therefore meets the limitation of the claims. It is also noted that the claims do not require that the sequences of the probes are not also complementary to a SARS-CoV in addition to being complementary to the "non-SARS-CoV infectious organisms". Therefore, Applicant's arguments are not persuasive regarding Shi or Marra. The rejections are maintained.

Relevant Prior art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Affymetrix Press release (May 6, 2003, pages 1-2) discloses a new GeneChip™ CustomSeq™ SARS Pathogen detection and resequencing array (p. 1).

Conclusion

All claims stand rejected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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